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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/616,283	07/14/2000	Timothy T. Goodnow	109. 111. 114	6499

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EXAMINER	
HINES, JANA A	
ART UNIT	PAPER NUMBER
1645	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/616,283	GOODNOW, TIMOTHY T.	
	Examiner	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 14-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicants amendment filed January 24, 2002 has been entered. Examiner acknowledges amendments to the specification. Claims 9-13 and 19-22 have been canceled. Claims 1, 7, 8, 14, 17 and 18 have been amended. Claims 1-8, and 14-18 are under consideration in this office action.

Withdrawal of Rejections

2. The rejection of claims 1-2, 4, 6-8 and 14-22 under 35 U.S.C. 102(b) as being anticipated by Young (US Patent 5,698,198) is withdrawn in view of applicants amendments and arguments.

The rejection of claims 3 and 5 under 35 U.S.C. 103(a) as being unpatentable over Young (US Patent 5,698,198) in view of Richards (US Patent 5,043,267) is withdrawn in view of applicants amendments and arguments.

The rejection of claims 1-8, and 14-18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicants amendments and arguments.

New Grounds For Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-8 and 14-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening for the presence of a clinically relevant amount of bacteria in a donor blood or blood product from a donor mammal for transfer to a recipient mammal comprising contacting a sample of the donor blood or blood product with a set of binding agents, wherein the set of binding agents are detectably labeled and it specifically bind to a gram-negative/positive antigen and determining the binding, does not reasonably provide enablement for a method for screening for the presence of a clinically relevant amount of bacteria in a donor blood or blood product from a donor mammal for transfer to a recipient mammal comprising contacting a sample of the donor blood or blood product with a set of binding agents, wherein the set of binding agents specifically bind to a gram-negative/positive antigen and determining the binding. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

The claims are drawn to a method for screening for the presence of a clinically relevant amount of bacteria in a donor blood or blood product from a donor mammal for

transfer to a recipient mammal comprising contacting a sample of the donor blood or blood product with a set of binding agents, wherein the set of binding agents specifically bind to a gram-negative/positive antigen and determining the binding of said agents for the presence or absence of the bacterial antigen.

However, the claims are rejected because the method does not recite positive steps necessary to determining whether binding has occurred which appears to be a critical step of the invention. The instant specification teaches binding agents being detectably labeled with reporter molecules such as those with enzymatic activity, radiolabel, fusion molecules, fluorogenic molecules, metal sols, particles and/or chromatic molecules (page 5 lines 6-8, page 6 lines 5-9). See also pages 29-31 lines 25-15 which teach a wide variety of detectable labels. Examples I, II and IV-VIII all teach the method using detectably labeled binding agents in a method to detect the presence of a clinically relevant amount of bacteria. In the alternative, Example III teaches agglutination assays wherein latex particles are coated with binding agents, however, the instant claims do not positively recite method steps drawn to the particle based immunoassay i.e., the binding agent are coated on particles.

The specification fails to teach examples of a set of binding agents specifically bind to a gram-negative/positive antigen and determining the binding of said agents for the presence or absence of the bacterial antigen without a detectable label yet perform the functions of the claims. The specification appears to make the conclusion that detectable labels are required to determine binding and/or presence of a bacterial

antigen. Therefore, the claims are only enabled for the use of detectably labeled binding agents.

Without a detectable label to indicate binding of the complex, one of ordinary skill in the art could not determine whether the binding agents bound bacteria in order to determine presence of bacteria. In view of specification that teaches the use of detectably labeled binding agents, undue experimentation would be required to locate de novo how to determine binding and detection of bacterial antigens. There is no guidance to enable one of ordinary skill in the art how to make, without undue experimentation, to determine the presence or absence of the bacteria wherein the set of binding agents are detectably labeled and it specifically bind to a gram-negative/positive antigen and determining the binding. Given the lack of guidance contained in the specification for detecting a bacterial antigen without a detectable label, one of skill in the art could not make or use the broad claimed invention without undue experimentation.

4. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 is confusing. The preamble and most of the steps of the claim is drawn to screening gram-negative bacteria, however the determining step recites determining the binding of gram-negative and gram-positive antigens. Thus, the claim is confusing in that it recites only one step drawn to the gram-positive step.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 3-6, 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan (EP 461, 462) in view of McLaughlin and Tadler et al.

Chan teaches an immunoassay to simultaneously detect the presence or amount of at least one antigen which may be present in a test sample which comprises contacting a test sample with solid support on which one or more antigens are immobilized as discrete test sites which determines antigen-antibody complexes (page 4 lines18-22). The antigen-antibody binding systems are detected by contacting the complexes with a conjugated signal general system which is capable of yielding a quantitatively measurable signal correlated to the signal of normal test sample to indicate antigen positive or antigen negative for the test sample (page 4 lines 18-27). Any number of immunoglobulins of one infectious agent or combinations of immunoglobulins to several infectious agents can be included on a single solid support and then analyzed in a single test procedure (page 5 lines 5-7). Test samples can be bodily fluids such as serum or plasma (page 5 lines 13-15). However, Chan does not teach a set of gram-negative and gram-positive binding agents that specifically bind gram-negative and gram-positive bacteria.

McLaughlin teaches methods and materials for the identification of lipopolysaccharide (LPS) producing microorganisms. The structure of LPS has been described in studies of gram-negative bacteria, wherein the middle region is a conserved region (col. 1 lines 30-35). The shared antigen is often a component of the LPS, thereby allowing detection of gram-negative microorganisms such as *Neisseria, Brucella, Escherichia, Salmonella* and the like (col. 2 lines 60-66 and col. 5 lines 10-22). One of the antigenic determinant sites includes the glyocolipid antigen associated with endotoxins or endotoxin-like molecules produced by gram-negative microorganisms (col. 4 lines 20-25). The immunological detection of an entire class of microorganism within a sample is taught (col. 2 lines 45-47). A clinical sample may be defined as body fluids or secretions such as blood, serum, saliva, stool, topical washing of skin or genitals, tissue samples or homogenates thereof (col. 5 lines 65-68). The antibodies can be used in any well-known immunological detection system, such as ELISA, or precipitation or agglutination assays (col. 5 lines 36-54). The authors teach several antibodies to lipid A and endotoxin glycolipids (Table 1). For instance, a clinical sample contains both Chlamydia and Neisseria; both organisms are detected by the capture antibody attached to the solid support (col. 6 lines 30-34). Once bound, the addition of two additional types of detectably labeled antibodies would permit simultaneous detection (col. 6 lines 34-36). Other variations employing colorimetric blending of two separate reaction products or the use of a radiometric/photo spectrometric combination is also possible (col. 6 lines 46-48).

Example 4 teaches a solid phase immunometric assay. Thus by using antibody of broad spectrum, it is possible to perform a single test for large number of LPS producing organisms by merely reacting the antibody with the clinical sample (col. 5 lines 29-34). However McLaughlin does not teach a set of gram-positive binding agents that specifically bind gram-positive bacteria.

Tadler et al., teach rapid recovery and identification of bacteria in blood would be important in patient management to prevent bacteremia which can present life-threatening situations for several patient populations (page 21). Tadler et al., teach sandwich immunoassay for the detection of lipoteichoic acid, (LTA) which is a major cell wall constituent of gram-positive bacteria from whole blood (abstract). Monoclonal antibodies to LTA were produced and many reacted exclusively with gram-positive bacteria (abstract). Nine monoclonal antibodies were selected that demonstrated reactivity to gram-positive bacteria but did not cross-react with the panel of gram-negative bacteria (page 22). Table 1 shows that characterization of anti-LTA monoclonal antibodies and its cross-reactivity with gram-positive bacteria. Further development of this assay may lead to rapid detection of LTA from other body fluids (abstract), however this assay is clearly useful in a clinical setting (page 24). Thus Tadler et al., teaches contacting a sample of blood with a set of binding agents; wherein specific binding occurs; and binding indicates the presence or absence of a clinically relevant amount of gram-positive bacteria in the blood sample and the identification of blood determined to have an absence of a clinically relevant amount of gram-positive bacteria.

It should also be noted, the recitation a method of screening of blood from a donor mammal for transfer to a recipient mammal, as recited in the claims has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference or additionally positively recited method steps between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Wherein the intended use is "useful for transfer to the recipient mammal". If the prior art method is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. There is no positively recited method step requiring the samples be transferred to a recipient mammal. Thus, the use of the sample is not considered as a limitation. Therefore, the prior art method is capable of performing the intended use, thus it meets the claim.

Therefore, it would have been prima facie obvious to modify the simultaneous multiple analyte detection immunoassay taught by Chan by incorporating a set of binding agents as taught by McLaughlin and Tadler et al., since McLaughlin teach antibodies which specifically bind to gram-negative bacteria in order to determine their

presence and/or absence while Tadler et al., teach well known binding agents that binds lipotechoic acid of gram-positive bacteria. Thus, one would have a reasonable expectation of success in utilizing a set of binding agents that bind to gram-negative and positive bacteria detection assays in a known multiple analyte simultaneous detection assays to test samples of blood. Moreover McLaughlin and Tadler et al, teaches samples suitable for practice of the method of detection to include whole blood, serum, and tissue and/or fluids.

6. Claims 2 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan, McLaughlin and Tadler et al., as applied to claims 1 and 14 above, and further in view of Chang et al., (US Patent 5,200,323). Chan, McLaughlin and Tadler et al., have all been discussed above, however none teach that in the absence of a clinically relevant amount of bacteria is transferred to a recipient mammal.

Chang et al., teach transfusion of blood from donor to recipient is a form of transplantation (col. 1 lines 8-10). However, bacterial infection, despite careful preparation from blood draws may contain a few bacteria (col. 2 lines 31-33). Thus it would be highly desirable to provide in vitro screening test that would be based on human blood or plasma to determine the safety of modified hemoglobin for humans prior to clinical use; to provide a bridge between animal testing and human clinical trials and to rule out potential problems before starting the clinical trials (col. 4 lines 10-30).

Therefore, it would have been prima facie obvious to modify the method of screening by using blood or blood product determined to have an absence of clinically

relevant amount of bacteria as taught by as taught by Chan, McLaughlin and Tadler et al., since Chang et al., teach it is beneficial to screen blood to prevent contamination. Thus, one would have a reasonable expectation of success in utilizing blood screened with in vitro screening assays to determine the safety of the blood prior to clinical use. Moreover Chan, McLaughlin and Tadler et al, all teach in vitro screening assays capable of determining the presence or absence of a bacterial antigen.

7. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chan (EP 461,462) in view of Tadler et al., (1989). Chan and Tadler have been discussed above, along with the preamble language and intended use recitation. However Chan did not teach a set of gram-positive binding agents that specifically bind gram-positive bacteria.

Therefore, it would have been prima facie obvious to modify the simultaneous multiple analyte detection immunoassay taught by Chan by incorporating a multiple binding agents as taught by McLaughlin, since McLaughlin teach antibodies which specifically bind to gram-negative bacteria in order to determine their presence and/or absence. Thus, one would have a reasonable expectation of success in utilizing a set of binding agents that bind to gram-negative detection assays in a known multiple analyte simultaneous detection assay to test samples of blood. Moreover McLaughlin uses samples suitable for practice of the method of detection to include whole blood, serum, and tissue and/or fluids.

8. Claims 8 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan (EP 461,462) in view of McLaughlin (US Patent 4,683,196). Chan has been discussed above, however Chan does not teach a set of gram-negative binding agents which specifically bind gram-negative bacteria. McLaughlin, has also been discussed above. Also the preamble language and intended use recitation has been discussed.

Therefore, it would have been prima facie obvious to modify the simultaneous multiple analyte detection immunoassay taught by Chan by incorporating a multiple binding agents as taught by McLaughlin, since McLaughlin teach antibodies which specifically bind to gram-negative bacteria in order to determine their presence and/or absence. Thus, one would have a reasonable expectation of success in utilizing a set of binding agents that bind to gram-negative detection assays in a known multiple analyte simultaneous detection assay to test samples of blood. Moreover McLaughlin teaches radiometric techniques, like Chan.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na A Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
April 8, 2002

Patricia A. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER